

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for cefoperazone content, sterility, pyrogens, moisture, pH, identity, and crystallinity (if it is not the lyophilized powder).

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(a) If the batch is packaged for repackaging or for manufacturing use:

(1) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.

(2) For sterility testing: 20 packages, each containing equal portions of approximately 300 milligrams.

(b) If the batch is packaged for dispensing:

(1) For all tests except sterility: A minimum of 10 immediate containers of the batch.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Cefoperazone content.* Proceed as directed in § 436.338 of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 10 milligrams of cefoperazone per milliliter.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 250 milligrams per milliliter.

(6) *Identity.* From the high-pressure liquid chromatograms of the sample and the cefoperazone working standard determined as directed in paragraph (b)(1) of this section, calculate the adjusted retention times of the cefoperazone in the sample and standard solutions as follows:

Retention time of cefoperazone =  $t_s - t_u$

where:

$t_s$  = Retention time of working standard measured from point of injection into the chromatograph until the peak maximum appears on the chromatogram; and

$t_u$  = Retention time of sample measured from point of injection into the chromatograph until the peak maximum appears on the chromatogram.

(7) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

[48 FR 790, Jan. 7, 1983; 43 FR 7439, Feb. 22, 1983; 48 FR 28250, June 21, 1983, as amended at 55 FR 11583, Mar. 29, 1990]

#### § 442.13 Cefotaxime sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefotaxime sodium is the sodium salt of 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-7-[(2-amino-4-thiazolyl) (methoxyimino)acetyl]amino]-8-oxo, [6*R*]-[6  $\alpha$ , 7  $\beta$ (*Z*)]-. It is so purified and dried that:

(i) Its potency is not less than 855 micrograms and not more than 1,002 micrograms of cefotaxime per milligram on an anhydrous basis.

(ii) Its moisture content is not more than 6.0 percent.

(iii) Its pH in an aqueous solution is not less than 4.5 and not more than 6.5.

(iv) It gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research; 10 packages, each containing approximately 500 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution

with solution 1 to the reference concentration of 2.0 micrograms of cefotaxime per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii), except prepare the working standard and sample solutions and calculate the potency of the sample as follows:

(a) *Preparation of the working standard solution.* Dissolve and dilute an accurately weighed portion of the cefotaxime working standard in sufficient distilled water to obtain a concentration of 1 milligram of cefotaxime per milliliter.

(b) *Preparation of sample solution.* Dissolve and dilute an accurately weighed portion of the sample in sufficient distilled water to obtain a concentration of 1 milligram of cefotaxime per milliliter (estimated).

(c) *Calculation.* Calculate the cefotaxime content in micrograms per milligram as follows:

$$\frac{\text{Micrograms of cefotaxime per milligram of sample}}{A_s \times W_u} = \frac{A_u \times P_a}{A_s \times W_u}$$

where:

$A_u$ =Absorbance of sample solution;

$P_a$ =Potency of working standard solution in micrograms per milliliter;

$A_s$ =Absorbance of working standard solution; and

$W_u$ =Milligrams of sample per milliliter of sample solution.

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(4) *Identity.* Proceed as directed in § 436.323 of this chapter, except prepare spotting solutions as follows: Prepare solutions of the sample and working standard, each containing 1 milligram of cefotaxime per milliliter in distilled water.

[50 FR 45109, Oct. 30, 1985, as amended at 55 FR 11583, Mar. 29, 1990]

#### § 442.13a Sterile cefotaxime sodium.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefotaxime sodium is the sodium salt of 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic

acid, 3-[(acetyloxy)methyl]-7-[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-8-oxo-, [6*R*]-[6*α*, 7*β*(*Z*)]-. It is so purified and dried that:

(i) Its potency is not less than 855 micrograms and not more than 1,002 micrograms of cefotaxime per milligram on an anhydrous basis. If it is packaged for dispensing, its content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefotaxime that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 6.0 percent.

(vi) Its pH in an aqueous solution is not less than 4.5 and not more than 6.5.

(vii) It gives a positive identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

(a) If the batch is packaged for repackaging or for use as an ingredient in the manufacture of another drug:

(1) For all tests except sterility: 10 packages, each containing approximately 1 gram.

(2) For sterility testing: 20 packages, each containing approximately 1 gram.

(b) If the batch is packaged for dispensing:

(1) For all tests except sterility: A minimum of 10 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay—(1) Potency.* Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately